REMARKS

Upon entry of the above amendment, claims 1-3 and 8-10 will be pending in the present application. Claims 4-7 have been canceled without prejudice or disclaimer. Claims 1, 3 and 10 have been amended.

Claims 1, 3 and 10 have been amended, for the sole reason of advancing prosecution. Applicants, by amending or cancelling any claims herein, make no admission as to the validity of any rejection made by the Examiner against any of these claims. Applicants reserve the right to reassert any of the claims canceled herein or the original claim scope of any claim amended herein, in a continuing application.

Claim 1 has been amended to incorporate the limitations of canceled claim 7. Support for amended claim 1 can be found throughout the specification and claims as originally filed. For example, please *see* the present specification at page 4, lines 6-11; page 5, lines 10-16; and original claim 7. Applicants respectfully submit that the amendment of claim 1 does not add any new matter within the meaning of 35 USC §132.

Independent claim 1 has been amended to recite "a patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive agent and oxybutynin and/or a pharmaceutically acceptable salt thereof, wherein the adhesive layer comprises at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein

the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule; and a styrene-isoprene-styrene block copolymer, wherein the weight ratio of the at least one acrylic polymer to the styrene-isoprene-styrene block copolymer is from 1:4 to 1:19." Claims 2, 3 and 8-10 each depend, either directly or indirectly, from claim 1.

Claims 3 and 10 have been amended to correct minor errors and to place them in proper U.S. format. No new matter has been added.

In view of the remarks set forth herein, further and favorable consideration is respectfully requested.

I. At pages 2-4 of the Official Action, claims 1-6 and 8-10 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Terahara et al. (WO 02/38139, using U.S. Publication No. 2004/0028724 as an English equivalent translation).

The Examiner asserts that it "would have been obvious to one of ordinary skill in the art to modify the weight ratio of content of the acrylic polymer to the rubber polymer to optimize the formation of the adhesive layer and sufficient skin permeability of the drug."

Applicant respectfully traverses this rejection of claims 1-6 and 8-10. The cited reference does not establish a *prima facie* case of obviousness against the presently pending claims.

To establish a prima facie case of obviousness, the PTO must satisfy three requirements. First, as the U.S. Supreme Court recently held in *KSR International Co.*

v. Teleflex Inc. et al., Slip Opinion No. 04-1350, 550 U.S. __ (April 30, 2007), "a court must ask whether the improvement is more than the predictable use of prior art elements according to their established functions. ...it [may] be necessary for a court to look to interrelated teachings of multiple patents; the effects of demands known to the design community or present in the marketplace; and the background knowledge possessed by a person having ordinary skill in the art, all in order to determine whether there was an apparent reason to combine the known elements in the fashion claimed by the patent at issue. ...it can be important to identify a reason that would have prompted a person of ordinary skill in the relevant field to combine the elements in the way the claimed new invention does... because inventions in most, if not all, instances rely upon building blocks long since uncovered, and claimed discoveries almost of necessity will be combinations of what, in some sense, is already known." (*KSR*, supra, slip opinion at 13-15). Second, the proposed modification of the prior art must have had a reasonable expectation of success, determined from the vantage point of the skilled artisan at the time the invention was made. *Amgen Inc. v. Chugai Pharm. Co.*, 18 USPQ 1016, 1023 (C.C.P.A 1970). Lastly, the prior art references must teach or suggest all the limitations of the claims. *In re Wilson*, 165 USPQ 494, 496 (C.C.P.A. 1970).

Further, the Supreme Court in *KSR* reiterated the framework for determining obviousness that was stated in *Graham v. John Deere Co.* 383 U.S. 1, 148 USPQ 459 (1966). The four factual inquiries that were recited in *Graham* are as follows: (1)

Determining the scope and contents of the prior art; (2) Ascertaining the differences between the prior art and the claims in issue; (3) Resolving the level of ordinary skill in the pertinent art; and (4) Evaluating evidence of secondary considerations, such as unexpected results. *Id.* As stated in MPEP 2141, secondary considerations such as unexpected results must be considered in every case in which they are present.

A. The Presently Claimed Invention

The presently claimed invention as exemplified by currently amended independent claim 1 is directed to:

> a patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive agent and oxybutynin and/or a pharmaceutically acceptable salt thereof, wherein the adhesive layer comprises at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule; and a styrene-isoprene-styrene block copolymer, wherein the weight ratio of the at least one acrylic polymer to the styrene-isoprene-styrene block copolymer is from 1:4 to 1:19

B. The Terahara *et al.* Reference

The Terahara *et al.* reference describes a transdermal preparation containing a drug in the form of an acid addition salt, and an adhesive layer comprising an acrylic polymer and a rubber polymer.

C. The Terahara et al. reference does not show all the elements of the pending claims, and thus cannot render these claims obvious

The presently pending claims are distinguishable from the cited reference. The reference does not contain all the elements of the presently pending claims, and thus

cannot render these claims obvious. Independent claim 1 recites "a patch comprising a backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive agent and oxybutynin and/or a pharmaceutically acceptable salt thereof, wherein the adhesive layer comprises at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule; and a styrene-isoprene-styrene block copolymer, wherein the weight ratio of the at least one acrylic polymer to the styrene-isoprene-styrene block copolymer is from 1:4 to 1:19."

More specifically, the Terahara *et al.* references fails to teach "at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer," as presently claimed. The Applicants note that the limitations of claim 7 have been incorporated into amended claim 1. Claim 7 was not included in the present rejection; thus, the Terahara *et al.* reference fails to teach or suggest the specific acrylic polymers recited in amended claim 1.

In view of the foregoing, Applicants submit that the Terahara *et al.* reference does not describe all of the elements recited in present claim 1, and thus cannot render present claims 1-3 and 8-10 obvious. Therefore, the Examiner is respectfully requested to reconsider and withdraw this rejection of claims 1-3 and 8-10.

D. No *prima facie* Case of Obviousness Has Been Established

There is no teaching in the cited reference which would motivate the skilled artisan to modify the transdermal preparation of the Terahara *et al.* reference to achieve the presently claimed transdermal patch. Without such a teaching, the skilled artisan would have absolutely no motivation to modify the teachings of this reference to arrive at the presently claimed patch. In particular, the Terahara *et al.* reference does not describe the presently claimed combination of components, namely a "backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive agent and oxybutynin and/or a pharmaceutically acceptable salt thereof, wherein the adhesive layer comprises at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule; and a styrene-isoprene-styrene block copolymer, wherein the weight ratio of the at least one acrylic polymer to the styrene-isoprene-styrene block copolymer is from 1:4 to 1:19."

In contrast, Example 1, shown at paragraph 0048 in the Terahara *et al.* reference, describes the use of the drug Procaterol hydrochloride and the acrylic polymer, methyl methacrylate-butyl methacrylate-dimethylaminoethyl methacrylate copolymer. Example 2, shown at paragraph 0050 in the Terahara *et al.* reference, describes the use of the drug Tizanidine hydrochloride, and the acrylic polymer and the rubber polymer in a ratio of acrylic polymer to rubber polymer of 2.3 to 1. Further,

Example 4, shown at paragraph 0054 in the Terahara *et al.* reference, describes the use of oxybutynin hydrochloride. However nowhere in the Terahara *et al.* reference is there any teaching that would lead the skilled artisan to arrive at the features required by the presently claimed patch. Accordingly, a *prima facie* case of obviousness has not been established.

E. The Unexpectedly Superior Properties of the Claimed Matrix

As stated in **MPEP 716.02**, the rationale to support a conclusion that the claims would have been obvious is that all the claimed elements were known in the prior art and one skilled in the art could have combined the elements as claimed by known methods with no change in their respective functions, and the combination would have yielded nothing more than predictable results to one of ordinary skill in the art at the time of the invention. In the present case, Applicants submit that the data set forth in the present specification establishes the unexpectedly superior, and thus unpredictable, results achieved by the presently claimed patch.

Applicants kindly bring the Examiner's attention to the unexpectedly superior properties of the presently claimed patch outlined in Tables 1 and 2, on pages 27 and 29, of the instant specification. The data clearly shows enhanced maximum skin permeation rates for the drug oxybutynin in those patch formulations that contain all the components as recited in the presently pending claims as compared to prior art patch formulations that do not include all of the presently claimed components. In particular, Examples 1-5, summarized in Tables 1 and 2, show drug permeation rates per unit area of skin achieved by the presently claimed patch. Comparative Examples 1-5, in Tables

1 and 2, show drug permeation rates for patch formulations lacking at least one of the components of the presently claimed patch. The data clearly shows that superior skin permeation rates and physical patch properties were achieved by the presently claimed patch, as compared to the drug permeation rates and physical properties achieved by patch formulations lacking at least one of the presently claimed components.

The Examiner asserts, at page 9 of the Official Action, that the data outlined in Tables 1 and 2 does not establish unexpectedly superior results because it is not commensurate in scope with the present claims. More specifically, the Examiner asserts that only one acrylic polymer and one rubber polymer are exemplified. Further, the Examiner asserts that the showing includes excipients that are not recited in the claims; therefore, any showing would need to demonstrate that the excipients have no bearing on the skin permeability results.

With regard to the Examiners assertion that the data is not commensurate in scope with the claims, claim 1 has been amended to recite: "at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule"; and "a styrene-isoprene-styrene block copolymer." Accordingly, it is submitted that the data are commensurate in scope with the presently pending claims.

Regarding the Examiners assertion as to excipients, Applicants again bring the Examiner's attention to Tables 1 and 2, on pages 27 and 29, of the present

specification. All of the patch formulations, listed in Table 1, include the components that the Examiner considers excipients. These excipients are all present in the ***same*** exact percentages. The only aspect of the patch formulations that changes is the ratio of the acrylic polymer to the rubber polymer. Further, Table 2 shows that Inventive Example 4 and Comparative Examples 4 and 5 all have the same excipients in the ***same*** percentages. Therefore, it submitted that this showing clearly demonstrates that it is the presently claimed patch formulation that is providing the superior permeability results, ***not*** the excipients themselves. As can be seen from Table 2, the presently claimed patch formulation of Inventive Example 4 achieved over twice the skin permeation as compared to that achieved by the patch formulations of Comparative Examples 4 and 5.

As to the Examiner's assertion that the comparative results are a mere difference in degree, Applicants respectfully submit that the results show more than a mere difference in degree. Both Tables 1 and 2 show that the maximum skin permeation rate achieved by the presently claimed patch formulations of the inventive examples, is substantially greater than the rate achieved by the patch formulations of the comparative examples. More specifically, Table 2 shows that Comparative Examples 4 and 5 have a maximum skin permeation rate of 11.7 and 9.7 $\mu g/cm^2/hr$, respectively. Inventive Example 4, which has the same excipients in the same percentages as Comparative Examples 4 and 5, has a maximum skin permeation rate of 28.8 $\mu g/cm^2/hr$. The permeation rate of the inventive example is ***more than double*** the permeation rate of each of comparative examples 4 and 5. Applicants submit that this

two-fold difference in permeation rates is more than a mere difference in degree and is unexpectedly superior as compared to the permeation rates achieved by the comparative patch formulations.

Accordingly, the data, outlined in Tables 1 and 2, on pages 27 and 29 of the present specification, establish the unexpectedly superior results achieved by the presently claimed patch. As such, the presently pending claims are not obvious over the Terahara *et al.* reference.

In view of the foregoing, Applicants submit that nothing in Terahara *et al.* renders the subject matter of present claims 1-3 and 8-10 obvious, within the meaning of 35 USC § 103. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection of claims 1-3 and 8-10.

II. At pages 4-5 of the Official Action, claims 1 and 4-10 have been rejected under 35 U.S.C. § 103(a) as being unpatentable over Chono et al. (EP 1 201 232).

The Examiner asserts that it would have been obvious to one of ordinary skill in the art to modify the weight ratio of content of the acrylic polymer to the rubber polymer to optimize the formation of the adhesive layer and sufficient skin permeability of the drug.

A. The Presently Claimed Invention

As previously discussed, the presently claimed invention as exemplified by currently amended independent claim 1 is directed to:

a patch comprising a backing layer and an adhesive layer disposed on the

backing layer and compounded with an adhesive agent and oxybutynin and/or a pharmaceutically acceptable salt thereof, wherein the adhesive layer comprises at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule; and a styrene-isoprene-styrene block copolymer, wherein the weight ratio of the at least one acrylic polymer to the styrene-isoprene-styrene block copolymer is from 1:4 to 1:19.

B. The Chono *et al.* Reference

The Chono *et al.* reference describes a patch formulation comprising a basic drug, an adhesive layer, and a backing layer for supporting the adhesive layer.

C. The Unexpectedly Superior Properties of the Claimed Matrix

As previously discussed, secondary considerations, such as unexpected results, are sufficient to overcome a *prima facie* case of obviousness. See **MPEP 716.02 and 2145.** Accordingly, Applicants again bring the Examiner's attention to the unexpectedly superior properties achieved by the presently claimed patch, as outlined in Tables 1 and 2, on pages 27 and 29, of the present specification.

The data clearly shows enhanced maximum skin permeation rates for the drug oxybutynin in those patch formulations that contain all the components as recited in the presently pending claims as compared to prior art patch formulations that do not include all of the presently claimed components. In particular, Examples 1-5, summarized in Tables 1 and 2, show drug permeation rates per unit area of skin achieved by the presently claimed patch. Comparative Examples 1-5, in Tables 1 and 2, show drug permeation rates for patch formulations lacking at least one of the components of the

presently claimed patch. The data clearly shows that superior skin permeation rates and physical patch properties were achieved by the presently claimed patch, as compared to the drug permeation rates achieved by patch formulations lacking at least one of the presently claimed components.

The Chono *et al.* reference does not describe any examples containing the combination of components recited by the presently pending claims, namely a "backing layer and an adhesive layer disposed on the backing layer and compounded with an adhesive agent and oxybutynin and/or a pharmaceutically acceptable salt thereof, wherein the adhesive layer comprises at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule; and a styrene-isoprene-styrene block copolymer, wherein the weight ratio of the at least one acrylic polymer to the styrene-isoprene-styrene block copolymer is from 1:4 to 1:19."

Further, there is no teaching anywhere in the Chono *et al.* reference that would motivate a person of ordinary skill in the art to arrive at the particular combination of components recited in the presently pending claims. In particular, Examples 2 and 3 in the Chono *et al.* reference show compositions comprising oxybutynin and a blend of rubber polymers, but lacking the acrylic polymer required by the presently pending claims. Examples 2 and 3 shown in the Chono *et al.* reference are analogous to Comparative Examples 1, 4 and 5 shown in the present specification because the

compositions disclosed in both sets of examples lack the presently claimed acrylic polymers. The data reported in Inventive Examples 1-5 of the present specification show the unexpectedly superior permeation rates achieved by the presently claimed patch as compared to the permeation rates achieved by compositions lacking an acrylic polymer.

As stated above in Section 1, the Examiner asserts, at page 9 of the Official Action, that the data outlined in Tables 1 and 2 does not establish unexpectedly superior results because it is not commensurate in scope with the claims. More specifically, the Examiner asserts that the examples that achieved the results only show one acrylic polymer and one rubber polymer. Further, the Examiner asserts that the showing demonstrates the inclusion of excipients, yet the excipients are not recited in the claims, therefore, any showing would need to demonstrate that the excipients have no bearing on the skin permeability results.

With regard to the Examiners assertion that the data is not commensurate in scope with the claims, claim 1 has been amended to recite: "at least one acrylic polymer selected from the group consisting of 2-ethylhexyl acrylate-N-vinyl-2-pyrrolidone-1,6-hexane glycol dimethacrylate terpolymer and 2-ethylhexyl acrylate-vinyl acetate copolymer, wherein the at least one acrylic polymer is substantially free of both carboxyl groups and hydroxyl groups in the molecule"; and "a styrene-isoprene-styrene block copolymer." Accordingly, it is submitted that the data are commensurate in scope with the claims.

Regarding the Examiners assertion as to excipients, Applicants again bring the

Examiner's attention to Tables 1 and 2, on pages 27 and 29, of the present specification. All of the patch formulations, listed in Table 1, include the components that the Examiner considers excipients. These excipients are all present in the ***same*** exact percentages. The only aspect of the patch formulations that changes is the ratio of the acrylic polymer to the rubber polymer. Further, Table 2 shows that Inventive Example 4 and Comparative Examples 4 and 5 all have the same excipients in the ***same*** percentages. Therefore, it submitted that this showing clearly demonstrates that it is the presently claimed patch formulation that is providing the superior permeability results, ***not*** the excipients themselves. As can be seen from Table 2, the presently claimed patch formulation of Inventive Example 4 achieved over twice the skin permeation as compared to that achieved by the patch formulations of Comparative Examples 4 and 5.

Regarding the Examiner's assertion that the comparative results are a mere difference in degree, Applicants respectfully submit that the results show more than a mere difference in degree. Both Tables 1 and 2 show that the maximum skin permeation rate is enhanced when the acrylic polymer and rubber polymer are present in the claimed ratios. More specifically, Table 2 shows that Comparative Examples 4 and 5 have a maximum skin permeation rate of 11.7 and 9.7 $\mu g/cm^2/hr$, respectively. Inventive Example 4, which has the same excipients in the same percentages as Comparative Examples 4 and 5 but contains different acrylic polymers, has a maximum skin permeation rate of 28.8 $\mu g/cm^2/hr$. The permeation rate of the inventive example is ***more than double*** the permeation rate of each of comparative examples 4 and 5.

Applicants submit that this difference in permeation rates is more than a mere difference in degree and shows unexpectedly superior results for the compositions containing the claimed components.

Accordingly, the data, outlined in Tables 1 and 2, on pages 27 and 29 of the present specification, establish the unexpectedly superior results achieved by the presently claimed patch. As such, the presently pending claims are not obvious over the Chono *et al.* reference.

In view of the foregoing, Applicants submit that nothing in Chono *et al.* renders the subject matter of present claims 1-3 and 8-10 obvious, within the meaning of 35 USC § 103. Thus, the Examiner is respectfully requested to reconsider and withdraw this rejection of claims 1-3 and 8-10.

III. Provisional Rejection of Claim 1 under the Judicially Created Doctrine of Obviousness-Type Double Patenting

The Official Action states that claim 1 is provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1, 8 and 13 of copending U.S. Patent Application Serial No. 10/469,612.

Applicants respectfully request that the Examiner hold this rejection in abeyance until such time as the Examiner indicates there is successful resolution of the claim rejections noted above. Applicants, at that time, will either address the rejection or file a terminal disclaimer over copending U.S. Patent Application No. 10/469,612.

CONCLUSION

Based upon the above remarks and amendment, the presently claimed subject matter is believed to be novel and patentably distinguishable over the prior art of record. The Examiner is therefore respectfully requested to reconsider and withdraw all rejections and allow all pending claims in this application. Favorable action with an early allowance of the claims pending in this application is earnestly solicited.

The Examiner is welcomed to telephone the undersigned attorney if she has any questions or comments. Please charge any fee deficiency or credit any overpayment to Deposit Account No. 14-0112.

Respectfully submitted,

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